neonatal onset multisystem inflammatory disease

Neonatal onset multisystem inflammatory disease (NOMID) is a disorder that causes persistent inflammation and tissue damage primarily affecting the nervous system, skin, and joints. Recurrent episodes of mild fever may also occur in this disorder.

People with NOMID have a skin rash that is usually present from birth. The rash persists throughout life, although it changes in size and location.

Affected individuals often have headaches, seizures, and vomiting resulting from chronic meningitis, which is inflammation of the tissue that covers and protects the brain and spinal cord (meninges). Intellectual disability may occur in some people with this disorder. Hearing and vision problems may result from nerve damage and inflammation in various tissues of the eyes.

People with NOMID experience joint inflammation, swelling, and cartilage overgrowth, causing characteristic prominent knees and other skeletal abnormalities that worsen over time. Joint deformities called contractures may restrict the movement of certain joints.

Other features of this disorder include short stature with shortening of the lower legs and forearms, and characteristic facial features such as a prominent forehead and protruding eyes. Abnormal deposits of a protein called amyloid (amyloidosis) may cause progressive kidney damage.

Frequency

NOMID is a very rare disorder; approximately 100 affected individuals have been reported worldwide.

Genetic Changes

Mutations in the *NLRP3* gene (also known as *CIAS1*) cause NOMID. The *NLRP3* gene provides instructions for making a protein called cryopyrin.

Cryopyrin belongs to a family of proteins called nucleotide-binding domain and leucine-rich repeat containing (NLR) proteins. These proteins are involved in the immune system, helping to regulate the process of inflammation. Inflammation occurs when the immune system sends signaling molecules and white blood cells to a site of injury or disease to fight microbial invaders and facilitate tissue repair. When this has been accomplished, the body stops (inhibits) the inflammatory response to prevent damage to its own cells and tissues.

Cryopyrin is involved in the assembly of a molecular complex called an inflammasome, which helps trigger the inflammatory process. Researchers believe that *NLRP3* mutations that cause NOMID result in a hyperactive cryopyrin protein and an inappropriate inflammatory response. Impairment of the body's mechanisms for controlling inflammation results in the episodes of fever and widespread inflammatory damage to the body's cells and tissues seen in NOMID.

In about 50 percent of individuals diagnosed with NOMID, no mutations in the *NLRP3* gene have been identified. The cause of NOMID in these individuals is unknown.

Inheritance Pattern

This condition is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder.

In almost all cases, NOMID results from new mutations. These cases occur in people with no history of the disorder in their family. A few cases have been reported in which an affected person has inherited the mutation from one affected parent.

Other Names for This Condition

- chronic infantile neurologic, cutaneous, and articular syndrome
- chronic infantile neurological, cutaneous and articular syndrome
- chronic neurologic, cutaneous, and articular syndrome
- CINCA
- CINCA syndrome
- infantile onset multisystem inflammatory disease
- IOMID syndrome
- NOMID
- Prieur-Griscelli syndrome

Diagnosis & Management

Genetic Testing

- Genetic Testing Registry: Chronic infantile neurological, cutaneous and articular syndrome
  https://www.ncbi.nlm.nih.gov/gtr/conditions/C0409818/

General Information from MedlinePlus

- Diagnostic Tests
  https://medlineplus.gov/diagnostictests.html
- Drug Therapy
  https://medlineplus.gov/drugtherapy.html
- Genetic Counseling
  https://medlineplus.gov/geneticcounseling.html
- Palliative Care
  https://medlineplus.gov/palliativecare.html
- Surgery and Rehabilitation
  https://medlineplus.gov/surgeryandrehabilitation.html

Additional Information & Resources

MedlinePlus

- Health Topic: Fever
  https://medlineplus.gov/fever.html

Genetic and Rare Diseases Information Center

- Chronic Infantile Neurological Cutaneous Articular syndrome
  https://rarediseases.info.nih.gov/diseases/1356/chronic-infantile-neurological-cutaneous-articular-syndrome

Additional NIH Resources

- NIH Pediatric Rheumatology Clinic
  https://www.niams.nih.gov/Health_Info/Pediatric_Diseases/

Educational Resources

- American College of Rheumatology
  http://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Cryopyrin-Associated-Autoinflammatory-Syndrome-CAPS-Juvenile
- Autoinflammatory Alliance: NOMID/CINCA
  http://www.nomidalliance.org/nomid.php
- Cleveland Clinic
  http://my.clevelandclinic.org/health/articles/periodic-fever-syndrome
- MalaCards: cinca syndrome
  http://www.malacards.org/card/cinca_syndrome
- Orphanet: CINCA syndrome
  http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=1451

Patient Support and Advocacy Resources

- Autoinflammatory Alliance
  http://www.nomidalliance.org/index.php
- National Organization for Rare Disorders (NORD)
  https://rarediseases.org/rare-diseases/neonatal-onset-multisystem-inflammatory-disease/
- RareConnect: Cryopyrin Associated Periodic Syndromes
  https://www.rareconnect.org/en/community/caps

ClinicalTrials.gov

- ClinicalTrials.gov
  https://clinicaltrials.gov/ct2/results?cond=%22neonatal+onset+multisystem+inflammatory+disease%22+OR+%22Cryopyrin-associated+Periodic+Syndromes%22+OR+%22Neonatal+Onset+Multisystem+Inflammatory+Disease%22

Scientific Articles on PubMed

- PubMed
  https://www.ncbi.nlm.nih.gov/pubmed?term=%28%28cinca%5BTIAB%5D%29+OR+%28neonatal+onset+multisystem+inflammatory+disease%5BTIAB%5D%29+OR+%28nomid%5BTIAB%5D%29+OR+%28infantile+onset+multisystem+inflammatory+disease%5BTIAB%5D%29%29+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+720+days%22%5Bdp%5D

OMIM

- CINCA SYNDROME
  http://omim.org/entry/607115

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